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Original Research Paper

Gastroenterology

ROLE OF SAROGLITAZAR IN THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER

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ABSTRACT

Background: A disorder of liver, Non-alcoholic fatty liver disease, has the potential to progress to chronic liver disease, which would then cause liver failure and portal hypertension. Although NAFL is likely to never progress in some people, it does take a very benign course in some and remains stable for years in others. The management of NAFL is empirical because the pathophysiology of this illness is still unknown. **Method:** A prospective observational study was conducted in the gastroenterology department for six months. Only 50 of the 100 patients assessed were analyzed with the intention to treat analysis. Present history, comorbidities, family history, social habits, HbA1C levels, body mass index (BMI), Blood Pressure monitoring, lipid profile, and liver function test results are the data that are gathered from patient records. Subjects who met the inclusion criteria were advised to consume the drug Saroglitazar for 6 months and were evaluated for all the baseline characteristics. **Results:** The mean age of participants was found to be 50.4 ± 11.78. Female patients (68 %) outnumbered male patients in terms of dominance (32%). After treatment with the drug, variables found to be significant were HbA1C, Total Cholestrol(TC), Low density Lipoprotein(LDL), Triglycerides(TG) and SBP. A total of 25 patients showed improvement in grade of Fatty Liver. Hence subjects showed a considerable improvement in their condition after receiving treatment with Saroglitazar. **Conclusion:** According to the findings of this study, Saroglitazar is also efficient in treating non-diabetic NAFL in addition to diabetic NAFL. This dual agonist showed a beneficial effect on controlling cardiovascular health and other risk factors which are known to accelerate disease progression.

KEYWORDS : Saroglitazar, NAFL, NAFLD

BACKGROUND:

Non-alcoholic fatty liver disease (NAFLD) is a clinicopathological syndrome that encompasses entire spectrum of fatty liver disease (ranging from fatty liver to staeatohepatitis, fibrosis and cirrhosis) where there is an accumulation of excess fat in liver in individuals without significant alcohol consumption. [1-4] While steatosis is usually associated with a benign prognosis, steatohepatitis and fibrosis may progress to cirrhosis.It develops insidiously and is a "Silent" disease because many people present with no or few symptoms until the disease has progressed.

NAFLD is a multifaceted condition.[1] For the sake of terminology, NAFLD is comprised of Nonalcoholic fatty liver (NAFL), Non-alcoholic steatohepatitis (NASH), Fibrosis and Cirrhosis.[3,4] NAFL is characterized by steatosis of the liver, involving greater than 5% of parenchyma, with no evidence of hepatocyte injury.[3,5] The excess fat is stored mainly as triglycerides.[2] NASH is defined by histologic terms, that is a necroinflammatory process whereby the liver cells become injured in a background of steatosis.[5] Although the natural history of NAFLD remains incompletely characterized, what is clear from the published data is a risk of progression to cirrhosis and HCC.[3, 6-10] However, whether there is a clear progression of NAFL to NASH is under active investigation, but early evidence suggests this could be the case.[3,4]

In terms of epidemiology, several studies have tried to quantify the true worldwide incidence of NAFL/NASH; however, due to extreme variations in study parameters and available testing, a clear and reliable occurrence rate is not currently available.[4,11] However, it is estimated that prevalence of nonalcoholic fatty liver disease (NAFLD) worldwide is approximately 25%.[11] It affects 33% of the general population and up to 70-75% of diabetes and obese patients in Western countries.[1,12,13] In fact, NAFLD has been projected, within the next 20 years, to become the major cause of liver related morbidity and mortality as well as a leading indication for liver transplantation. [3,14]

There is no known exact cause of NAFL. However, some risk factors include DM-Type 2, Dyslipidemia, Obesity, Metabolic Syndrome, Hypothyroidism, Menopause, PCOS, Obstructive Sleep Apnea, etc.A diagnosis of NAFLD should be made only in the absence of excessive alcohol intake (defined as alcohol consumption of more than 20 g/day for men and more than 10 g/day for women), and other secondary causes of hepatic fat accumulation such as viral hepatitis, autoimmune hepatitis; hereditary or metabolic liver diseases such as Wilson's disease Lypodystrophic disease, Hypobetalipoproteinemia, Weber-Christian disease, Wolman's disease, Cholesterol ester storage disease, Hemochromatosis; Drugs such as Corticosteroids, Estrogens , NSAID, Calcium antagonists, Amiodarone, Tamoxifen,Tetracycline, Clorochine, Perhexiline-maleate, Anti-retrovirals; Environmental toxins; Extrahepatic conditions such as Cardiac failure, IBD and other intestinal diseases, Intestinal bacterial overgrowth syndrome, Pregnancy, Neoplastic diseases; Nutritional such as Jejuno-ileal bypass, Total parenteral nutrition, Prolonged starvation, Protein malnutrition; etc.[15,16]

The most prevalent treatment to stop the progression is aimed at dietary modification and lifestyle changes.[17] Although NAFLD represent a major burden to the patient and the supporting health system, there is currently no approved pharmacotherapy targeting the disease, emphasizing the current need for novel intervention strategies.[18] Insulin sensitizers (metformin and thiazolidinediones, such as pioglitazone) and liraglutide are not specifically recommended for NAFL as they do not directly improve the liver condition. They can be indicated for diabetic individuals, after a careful assessment of risks, to reduce insulin resistance and risks of complications.[4,15] Indeed, the side effects associated with thiazolidinedione medications, which include

osteopenia, increased fracture risk retention, congestive heart failure, bladder cancer, and long-term weight gain, have limited their adoption.[19] According to AASLD guidelines, "omega-3 fatty acids should not be used as a specific treatment of NAFL or NASH, but they may be considered to treat hypertriglyceridemia for patients with NAFL".[4] Saroglitazar is a potent and predominantly Peroxisome Proliferator Activated Receptor (PPAR)- alpha agonist with moderate PPAR-gamma agonistic activity. PPARs are nuclear lipid-activated transcription factors that regulate the expression of various genes involved in the control of lipid and lipoprotein metabolism, glucose homeostasis and inflammatory processes. The pharmacological effects of saroglitazar were extensively evaluated in various preclinical models. Saroglitazar showed both anti-dyslipidemic and anti-diabetic effects mainly mediated via activation of PPAR□ and PPAR□ respectively. This study focuses on the role of the drug Saroglitazar in the treatment of NAFL.

MATERIALS AND METHODS:

Study Population :

This prospective, observational study was carried out at the Department of Gastroenterology in a Tertiary Care Hospital in Hyderabad for a period of six months. A total of 50 of the 100 patients assessed were analyzed with the intention to treat analysis. Study protocol was approved by Institutional Ethics Committee, Deccan College of Medical Sciences, Kanchanbagh, Hyderabad. Patients with NAFL were prescribed Saroglitazar 4mg twice daily before food by treating physician as per standard of care in the outpatient department. Patient data was procured after taking Informed Consent using Patient's case sheet, History interview from the patient/ patient's representative, patient's medical record and laboratory investigations. Inclusion Criteria were - Patients of age 18-75 yrs; both genders; Patients with alcohol consumption of less than 20 g/day for men and less than 10 g/day for women; NAFL patients with or without any comorbidity. Exclusion Criteria were - Paediatric patients; Patients with incomplete lab data; Pregnant and lactating women; Patients with Type-1 Diabetes Mellitus, viral hepatitis, Autoimmune Hepatitis, Hereditary or Metabolic liver diseases such as Wilson's disease, Lypodystrophic disease, Hypobetalipoproteinemia, Weber-Christian disease, Wolman's disease, Cholesterol ester storage disease, Hemochromatosis, etc; Extrahepatic conditions such as Cardiac failure, Chronic Kidney Disease, Uncontrolled Thyroid Disease, IBD and other intestinal diseases, Intestinal bacterial overgrowth syndrome, Neoplastic diseases; Nutritional such as Jejuno-ileal bypass, Total parenteral nutrition; use of drugs with hepatotoxicity/hepatic fibrosis (sodium valproate, antiretroviral drugs, amiodarone, anabolic steroids, clorochine, tetracycline, etc.); significant alcohol consumption of more than 20 g/day for men and more than 10 g/day for women; Patients who do not comply to participate in the study. Assessment Of Patient was done after every 4-5 weeks.

Measurements And Analytical Determinations:

Baseline Investigations include Weight; BMI; SBP; DBP; HbA1C; TC; LDL; HDL; VLDL; TG; USG Grade (Grade-0,1,2,3).Compliance to treatment was assessed by using Morisky Medication Adherence Scale(MMAS).

Statistical Analysis:

Statistical evaluations were performed using SPSS Software Version 22. Means and standard deviations are provided for continuous variables whereas numbers and percentages for qualitative variables. Analysis for single parameters were performed using analysis coupled Student-t test and Mann Whitney test. The 5% level was used to identify differences in between groups that were of statistical significance (P value <0.05).

Ethical Standards:

All procedures followed were in accordance with Institutional Ethics Committee, Deccan College of Medical Sciences, Kanchanbagh, Hyderabad.

RESULTS:

A total of 100 patients were assessed for eligibility, out of which only 60 patients were enrolled and the other 40 patients were excluded as they did not meet the study criteria.Later, 10 patients were also excluded as 6 of them were lost to follow up and 4 were irregular at treatment.Hence a total of 50 patients were included in the study.

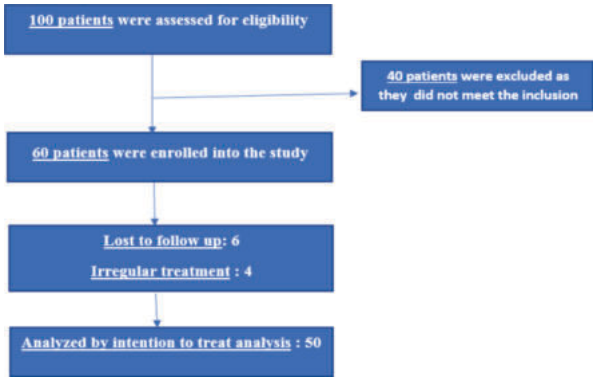


Figure 1: Flow of particiants in the study

Table 1: Demographic Profile Of Patients(n=50). Data Are Expressed As mean±S.D or number(%).

Characteristics	Mean/ n(%)
Age	50.4±11.78
Male	16 (32%)
Female	34 (68%)
Weight(Kg)	71.39±31.61
BMI(Kg/m^2)	25.68±11.67
Normal BMI	19 (38%)
Overweight	29 (58%)
Obese	2 (4%)
SBP	128.41±45.32
DBP	85.4±8.85
Comorbidities and their duration:	
NO. OF DIABETIC PATIENTS	18 (36%)
Duration of DM	1.66±3.59
NO. OF HYPERTENSION PATIENTS	17 (34%)
Duration of HTN	2.79±4.93
NO. OF DYSLIPIDEMIA PATIENTS	5 (10%)
Duration of dyslipidemia	0.2±0.83
NO. OF OBESE PATIENTS	2 (4%)
Duration of obesity	0.16±0.81

BMI, Body Mass Index; SBP,Systolic Blood Pressure; DBP,Diastolic Blood Pressure; DM,Diabetes Mellitus; HTN,Hypertension.

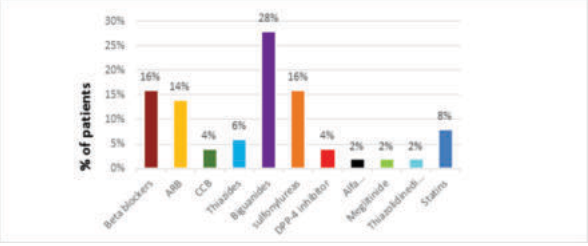
Demographic details of patients are given in Table 1. The mean age of participants was 50.4 ± 11.78. Females were found to be more than males in the subjects involved, which is 68% and 32%, respectively. The average duration of the subjects suffering from hypertension (2.79 ± 4.93) is more than diabetes (1.66 ± 3.59), dyslipidemia (0.2 ± 0.83), and obesity (0.16 ± 0.81).

Table-2. Pre-enrollment Medication Details Of Patients(n=50).

ARB, Angiotensin Receptor Blocker; CCB, Calcium Channel Blocker

No. of drugs	n(%)
Anti-Hypertensive Drugs:	
Beta blockers	8(16%)
ARB	7(14%)
CCB	2(4%)
Thiazides	3(6%)

Anti-Diabetic Drugs:	
Biguanides	14(28%)
Sulfonylureas	8(16%)
DPP-4 inhibitor	2(4%)
Alfa glucosidase inhibitor	1(2%)
Meglitinide	1(2%)
Thiazolidinedione	1(2%)
Drugs for Dyslipidemia:	
Statins	4(8%)



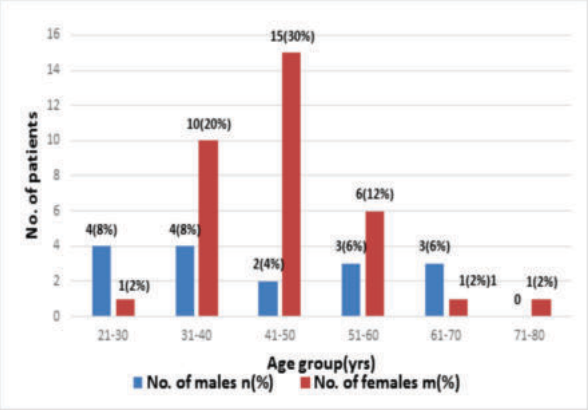
Graph-1. Pre-enrollment medication details of patients(n=50).

ARB, Angiotensin Receptor Blocker; CCB,Calcium Channel Blocker

In Table 2 and Graph 1, Pre-enrollment medication details of patients is shown. Most of the patients were taking Biguanides (28%), Sulfonylureas (16%), Beta blockers (16%), followed by ARB(14%), Statins(8%), Thiazides(6%), CCB(4%), DPP-4 inhibitor(4%), Alfaglucosidase Inhibitor(2%), Meglitinide(2%), Thiazolidinedione(2%).

Table-3. Distribution Of Patients Based On Age Group

Age Group (yrs)	No. of males n(%)	No. of females m(%)
21-30	4(8%)	1(2%)
31-40	4(8%)	10(20%)
41-50	2(4%)	15(30%)
51-60	3(6%)	6(12%)
61-70	3(6%)	1(2%)
71-80	0	1(2%)
Total	16(32%)	34(68%)

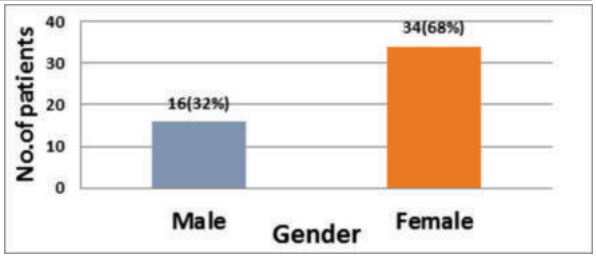


Graph-2. Distribution Of Patients Based On Age Group

In Table 3, Graph 2, Distribution of patients based on Age Group is shown. Number of male patients (8%) were more between the age group 21-40 and number of female patients (30%) were more between the age group 41-50 . Females were found to be more than males in the subjects involved, which is 68% and 32%, respectively.

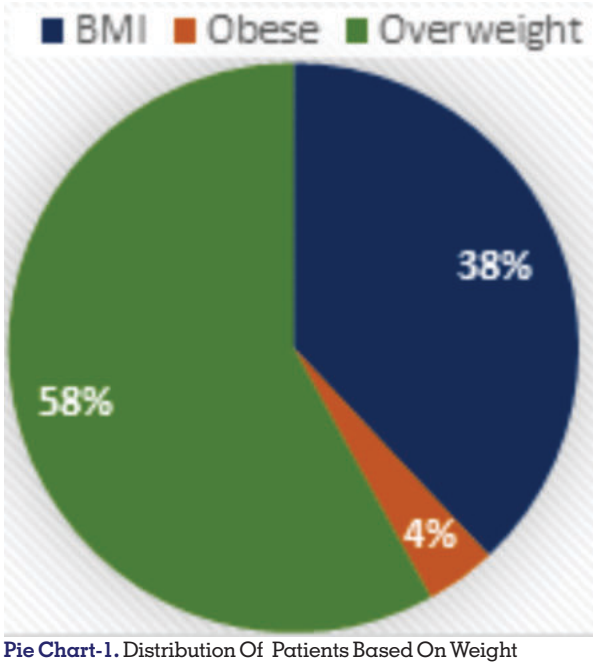
Table-4. Distribution Of Patients Based On Gender

No. of patients (N)	No. of males n(%)	No. of females m(%)
21-30	16(32%)	34(68%)



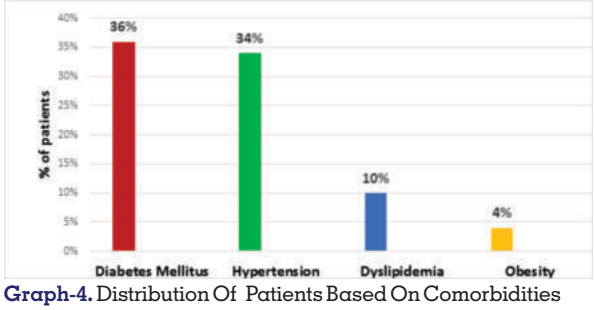
Graph-3. Distribution Of Patients Based On Gender

In Table 4, Graph 3 Distribution of patients based on Gender is shown. Females were found to be more than males in the subjects involved, which is 68% and 32%, respectively.



Pie Chart-1. Distribution Of Patients Based On Weight

From the data obtained, Pie Chart 1 shows that 58% of patients were found to be over weight and 4% of patients were found to be obese.



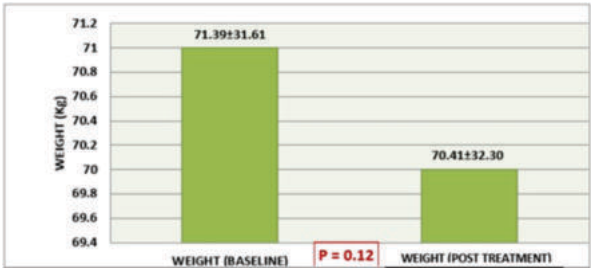
Graph-4. Distribution Of Patients Based On Comorbidities

From the data obtained, Graph 4 shows that number of diabetic patients (36%) are highest, followed by hypertension (34%), Dyslipidemia(10%) and Obesity(4%)

Table-5. Comparison of baseline and Post-treatment parameters(n=50). Data are expressed as mean±S.D. BMI,Body Mass Index; SBP,Systolic Blood Pressure; DBP,Diastolic Blood Pressure; TC,Total Cholestrol; LDL,Low density Lipoprotein; HDL,High density Lipoprotein; VLDL,Very Low Density Lipoprotein; TG,Triglycerides

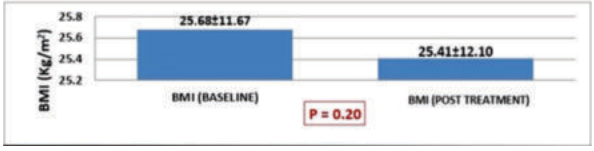
Variables	BASELINE	POST TREATMENT	P value
Weight (Kg)	71.39±31.61	70.41±32.30	0.12
BMI(Kg/m^2)	25.68±11.67	25.41±12.10	0.20
SBP (mmHg)	128.41±45.32	123.41±47.18	0.05*

DBP (mmHg)	85.4±8.85	82.2±7.15	0.23
HbA1C (%)	7.2±0.65	6.3±0.87	0.02*
TC (mg/dl)	171.92±62.52	159.3±60.40	0.008*
LDL (mg/dl)	105.06±45.02	96.85±30.41	0.05*
HDL (mg/dl)	45.25±15.07	40.81±10.47	0.18
VLDL (mg/dl)	30.56±13.07	30.21±14.47	0.18
TG (mg/dl)	171.91±13.07	139.78±14.47	0.02*



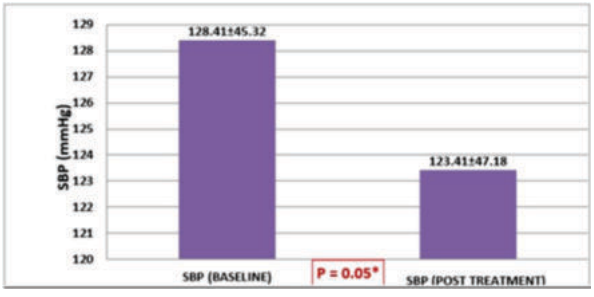
Graph-5. Comparison Of Weight At Baseline And Post Treatment

Graph 5 shows that on comparison of weight at baseline and after treatment, change in mean weight was found to be insignificant (P=0.12), with 71.39 ± 31.61 at baseline and 70.41 ± 32.30 after treatment.



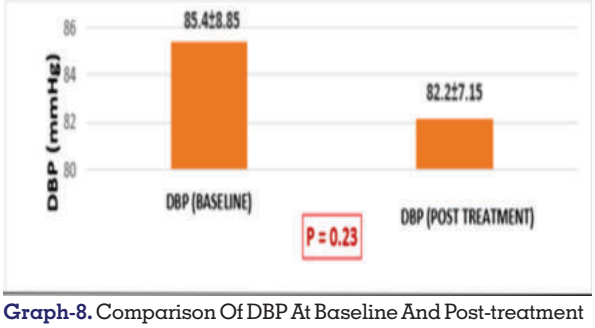
Graph-6. Comparison Of BMI At Baseline And Post-treatment

Graph 6 shows that on comparison of BMI at baseline and after treatment, change in mean BMI was found to be insignificant (P=0.20), with 25.68 ± 11.67 at baseline and 25.41 ± 12.10 after 20 treatment.



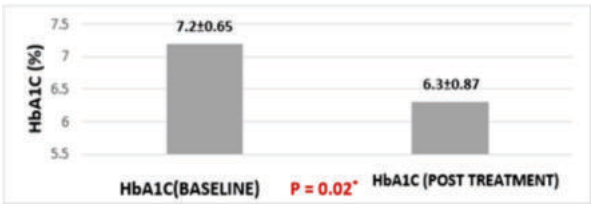
Graph-7. Comparison of SBP at Baseline and Post-treatment

Graph 7 shows that on comparison of SBP at baseline and after treatment, change in mean SBP was found to be significant (P=0.05), with 128.41±45.32 at baseline and 123.41±47.18 after treatment.



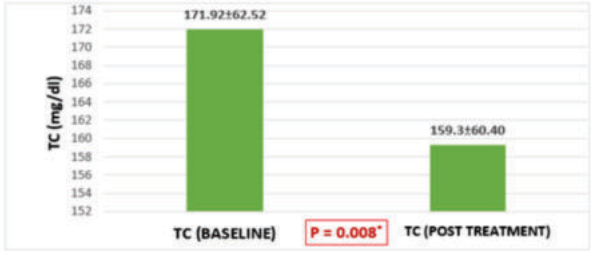
Graph-8. Comparison Of DBP At Baseline And Post-treatment

Graph 8 shows that on comparison comparison of DBP at baseline and after treatment, change in mean DBP was found to be insignificant (P=0.23), with 85.4±8.85 at baseline and 82.2±7.15 after treatment.



Graph-9. Comparison of HbA1C at Baseline and Post-treatment

Graph 9 shows that on comparison comparison of HbA1C at baseline and after treatment, change in mean HbA1C was found to be significant (P=0.02), with 7.2±0.65 at baseline and 6.3±0.87 after treatment.

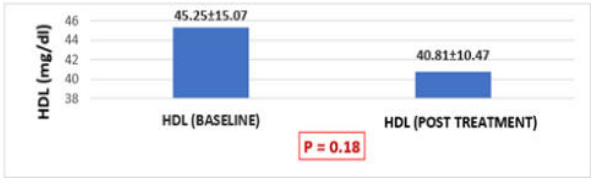


Graph-10. Comparison Of TC At Baseline And Post-treatment

Graph 10 shows that on comparison comparison of TC at baseline and after treatment, change in mean TC was found to be significant (P=0.008), with 171.92±62.52 at baseline and 159.3±60.40 after treatment.

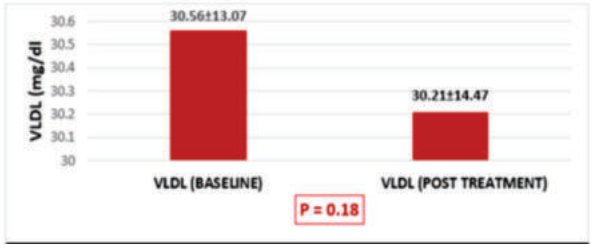
Graph-11. Comparison of LDL at Baseline and Post-treatment

Graph 11 shows that on comparison comparison of LDL at baseline and after treatment, change in mean LDL was found to be significant (P=0.05), with 105.06±45.02 at baseline and 96.85±30.41 after treatment.



Graph-12. Comparison of HDL at Baseline and Post-treatment

Graph 12 shows that on comparison comparison of HDL at baseline and after treatment, change in mean HDL was found to be insignificant (P=0.18), with 45.25±15.07 at baseline and 40.81±10.47 after treatment.



Graph-13. Comparison Of VLDL At Baseline And Post-treatment

Graph 13 shows that on comparison comparison of VLDL at baseline and after treatment, change in mean VLDL was found to be insignificant (P=0.18), with 30.56±13.07 at baseline and 30.21±14.47 after treatment.

Graph-14. Comparison Of TG At Baseline And Post-treatment

Graph 14 shows that on comparison comparison of TG at baseline and after treatment, change in mean TG was found to be significant (P=0.02), with 171.91±13.07 at baseline and 139.78±14.47 after treatment.

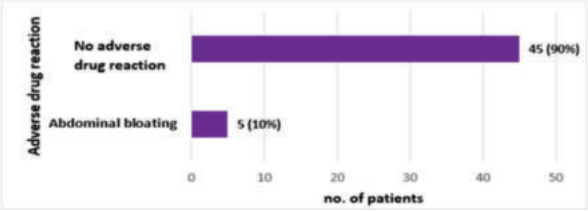
Table-6. Comparison Of USG Grades At Baseline And Post-treatment

Variables	USG Grade (BASELINE)	USG Grade (POST TREATMENT)
USG GRADE 0	0(0%)	20(40%)
USG GRADE 1	45 (90%)	5(10%)
USG GRADE 2	5 (10%)	0(0%)
USG GRADE 3	0 (0%)	0(0%)

Table 6 showas that at baseline, 45 patients(90%) had Grade-1 Fatty liver and 5 patients(10%) had Grade-2 Fatty liver but after treatment, fatty liver got resolved in 20 patients(40%) and Grade-2 of fatty liver got reduced to Grade-1 in 5 patients(10%), with a total of 25 positive results with the drug Saroglitazar.

Table-7. AdverseDrug Reaction(n=50)

Adverse Drug Reaction	n (%)
Abdominal bloating	5 (10%)
No adverse drug reaction	45 (90%)



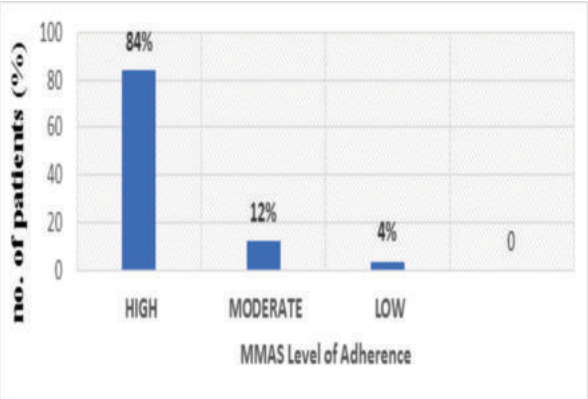
Graph-15. Adverse Drug Reaction

Table 7, Graph 15 shows that minor adverse drug reaction was reported in this study like abdominal bloating(10%)

Table-8. MMAS of Patients(n=50)

MMAS Level of Adherance	n (%)
High [>8]	42 (84%)
Moderate [6-8]	6 (12%)
Low [<6]	2(4%)

MMAS,Morisky Medication Adherence Scale



Graph-15. MMAS of Patients
MMAS, Morisky Medication Adherence Scale

Graph 15 shows that compliance to treatment was assessed using Morisky Medication Adherence Scale with many patients falling under High level of adherence category (80%) followed by moderate(12%) and low(4%).

DISCUSSION:

The present study reports the efficacy of Saroglitazar in improving Fatty liver, Dyslipidemia and Glycemic control, Hypertension and Obesity in NAFL patients. NAFLD as a public health challenge parallels the global upsurge for food intake, increase in per capita income, sedentary lifestyle, increasing body mass index and finally is an expression of an excess of caloric intake over expenditure by an individual.[20]

Saroglitazar, a dual α/γ agonist, has a well-established role in the management of DD.[14,21-23] Recently, Saroglitazar has stimulated interest of physicians for treatment of NAFLD due to its dual effect in improving dyslipidemia and insulin sensitivity. PPARα agonists play role in regulating fatty acid transport, β-**oxidation and modulation of inflammatory genes while** PPARγ agonists are strong insulin sensitizers regulating glucose and lipid metabolism.[1]. A clinical study has shown that saroglitazar (2-4 mg) decreases both the plasma atherogenic index and non-HDL/HDL ratio.[24] This demonstrates that saroglitazar lowers cardiovascular disease-related predictive lipid biomarkers.

The mean age of patients was 50.4±11.78. This could be due to aspects such as frailty, multimorbidity, polypharmacy and also with aging, the liver undergoes substantial changes in structure and function that are associated with significant impairment of many hepatic metabolic and detoxification activities.[25] Number of male patients (8%) were more between the age group 21-40 and number of female patients (30%) were more between the age group 41-50 . In males, NAFLD tends to increase from younger to middle-aged groups of individuals and the prevalence of disease begins to decline at the age of 50 or 60. This has been defined as an "inverted U shaped curve". Of interest, a study by Nakajima, although conducted in a restricted series of liver biopsies, was nevertheless able to demonstrate that advancing age was inversely correlated with steatosis.[26]On comparison of gender, Female patients (68%) were dominant than Male patients (32%). Hormonal changes have consistently been proposed to account for the varying prevalence rates of NAFLD in either gender. Consistent with a protective role of estrogens, during their fertile period, women tend to be spared from NAFLD compared to men. However, although they tend to develop the disease approximately 10 years later than men, post-menopausal women are no longer spared from NAFLD.[27] Insignificant reduction of weight and Body Mass Index could be because participants calorie intake is equal to or higher than his calorie use.

As expected, a favourable effect of Saroglitazar on lipid profile was noted in our study. After treatment, serum TG significantly reduced from 171.91±13.07 mg/dL to 139.78±14.47 mg/dL. Other parameters like LDL, total cholesterol also showed significant improvement. HDL and VLDL were insignificant in improvement.

HbA1c was used to assess the glycemic control. HbA1c is involved in pathogenesis of NAFLD through various pathways, so improvement in HbA1c also has positive impact on NAFLD[28]. Saroglitazar has been reported to provide significant reduction in HbA1c in DD patients.[14, 21-23, 29] In our study too, we observed a significant reduction in HbA1c from 7.2±0.65 to 6.3±0.87 with Saroglitazar.

Although there is no current well established relation between Hypertension and Fatty Liver; no current well established role of Saroglitazar in treating Hypertension; this study showed significant reduction of Systolic Blood Pressure(SBP) from

128.41±45.32 to 123.41±47.18. This finding paves a way for future studies on pathophysiologic association of Non-Alcoholic Fatty Liver with Hypertension as a risk factor or cause.

Assessment of change in hepatic steatosis is important aspect of assessing response to therapy in NAFL. Abdominal ultrasonography is often the first-line investigation for diagnosis of fatty liver. MR-PDFF is another technique to quantitatively assess liver fat. In a recent study, there was > 30% reduction in liver fat content measured by MR-PDFF, after treatment with Saroglitazar.[19] Although MRI-PDFF has shown to be superior than Ultrasonography, the former is limited by cost and availability.[30] In concordance with above study, we observed significant reduction of Fatty liver after 20 weeks of Saroglitazar treatment, suggesting improvement in hepatic steatosis. Sarin et al. also reported improvement in steatosis and inflammation on liver biopsy with Saroglitazar treatment.[31]

At baseline, 45 patients(90%) had Grade-1 Fatty liver and 5 patients(10%) had Grade-2 Fatty liver but after treatment with Saroglitazar, fatty liver got resolved in 20 patients(40%) and grade of fatty liver got reduced in 5 patients(10%), with a total of 25 positive results.

Minor adverse drug reaction like Abdominal Bloating(10%) was reported in our study, but none required treatment.

Compliance to treatment was assessed using Morisky Medication Adherence Scale with many patients falling under High level of adherence category (80%) followed by moderate(12%) and then low(4%).

Our study has few limitations, this study is not a randomized, placebo controlled trial, with no control group.Not conducting a liver biopsy could be considered another limitation, but as this study was an observational study in the outpatient setting , performing a liver biopsy was not possible, as it is rarely done for assessing fibrosis/steatosis in NAFLD patients in the real world study.The use of other concomittant anti-hypertensive, anti-diabetic and dyslipidemic drugs in our study is unlikely to affect the results, as the patients enrolled in this study were already on these drugs since past few/many months, and these were continued in the same doses during the study period. Moreover, there is no convincing data that existing anti-hypertensive, anti-diabetic and dyslipidemic drugs are effective in improving steatosis in NAFL.

CONCLUSION:

There is a necessity for developing a pragmatic approach for the better treatment of the condition of NAFL as the disease progression associated with the risk factors makes it vulnerable in the end stage. A holistic approach to halting the effect of the associated threats is the most prominent way to reduce the negative outcomes. A dual agonist of PPAR like saroglitazar showed a high impact on lowering blood pressure, lipid, and blood sugar profiles. Invariably, it diminishes all the ways through which a high chance of fat deposition can occur. However, a comprehensive, multi-sector approach is required to develop solid evidence on the most outstanding effects of saroglitazar on fat deposition regulation. Future studies can also highlight the effective duration of treatment required to achieve those effective changes.

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